UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,176	07/02/2003	Neng-Yang Shih	CN01576K1	5228

24265 7590 11/10/2004

SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
2000 GALLOPING HILL ROAD
KENILWORTH, NJ 07033-0530

EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 11/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,176	SHIH	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *23 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *19-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group I, species example 56 in the reply filed on Aug. 23, 2004 is acknowledged. The traversal is on the grounds that a reference was not received by applicants and the examiner has not shown why the searches are not coextensive and burdensome. This is not found persuasive because if the reference was missing in the mailing, applicants should have called the examiner for a copy. A copy is hereby attached again. In the restriction requirement, it has been clearly delineated the "classes" for which the groups would be classified and clearly conveyed that due to the enormous number of compounds or composition encompassed by the claims, a determination of a subclass was not possible without a species election. As it was delineated that group I is class 546 compounds, group II is in classes 540/544 depending on species election. For class 546, there are 563 subclasses, for class 540, there are 612 subclasses, for class 544 there are 410 subclasses. Thus, the burden of searching the enormous scope without restriction has been clearly conveyed to the applicants. In addition, the nonelected "core" such as pyrrolidinylpyrrolidine has adrenergic blocking activity (CA 65:6506), the pyrrolidinyltriazolyl core has anti-HIV activity (CA 129:260395). Applicants provided no factual evidence mere allegation. Applicants attention is drawn to that group VII is drawn to "kit" or medicinal packaging which is classified in a completely "unrelated" class 206 which is examined by a different group and art unit completely independent and distinct from the compound per se art.

The requirement is still deemed proper and is therefore made FINAL.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is *presented prior to* final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be **allowable**, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim or which do not meet all criteria for patentaility including the requirements of 35 U.S.C. 101, 102, 103 and 112 will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai; In re Brouwer and 35 U.S.C.§ 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include all the limitations of the product claims. *Applicants are reminded of propriety of process of use claims in consideration of the "reach-trough" format, which is drawn to mechanistic, receptor binding or enzymatic functionality. Reach through*

claims are considered lacking of descriptive and enabling support from the specification. Thus, rejoinable process of use claims are those with particular disease named with efficacy support from the specification for treating the particular disease. In the instant case, none of the compounds disclosed in the specification provided any in vivo data for the disclosed foot tapping test. The foot tapping test has been evidenced to be supportive for treating emesis only. The rejoinable process thus must be supported by factual evidence and limited to treating emesis. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01. Filing of appropriate terminal disclaimer in anticipation of a rejoinder may speed prosecution and the process of rejoinder.

Claims 10-17 and claims 1-9, 18 reading on claims 10-17 n2+n3 =2, are examined. Claims 19-35 and the remaining subject matter of claims 1-9, 18 are withdrawn from consideration per 37 CFR 1.142(b)

2. Claim18 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Please note that claim 18 is self conflicting because claims 18 is a "pharmaceutical" composition yet without a dosage limitation. Pharmaceutical composition by definition can not be either ineffective nor toxic. Therefore, it is recommended that the term "therapeutically effective amount" be incorporated into the claim.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et al. US 5,760,018 in view of Patani et al.

Determination of the scope and content of the prior art (MPEP §2141.01)

Baker et al. '018 is analogous art as the instant as piperidinyl compounds being tachykinin antagonists. Baker et al. '018 disclosed analogous compound as the claims see col. 4-6, generic description, especially col. 5 line 57 i.e.R11 is 2-pyrrolidinyl, and exemplified the structurally analogous compounds of the claims, see col. 22 example 8 , col. 26, example 17.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art is that instead of an N-CO amide linkage between the piperidinyl ring and the pyrrolidinyl ring, examples 22 and 26 have the CO-CH2 linkage. COCH2 linkage has been well recognized in the art as the "bioisoster" of the NCO amide linkage (see Patani p.3170, table 48).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would be motivated to modify the known and proven compound of the prior art with the well known conventional bioisosteric replacement since bioisosteric modification has been suggested by artisan in the field to be a rational approach in drug design (see Patani et al. whole article) and such modification is often considered to be qualitative and intuitive (p.3147), thus, prima facie obvious.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et al. US 5,760,018 or Harrison et al. US 5,620,989 supplemented with CA 122:81123 in view of Patani et al.

Determination of the scope and content of the prior art (MPEP §2141.01)

Baker et al. '018 and Harrison are analogous art as the instant as piperidinyl compounds being tachykinin antagonists. Baker et al. '018 disclosed analogous compound as the claims see col. 4-6, generic description, especially col. 5 line 57 i.e.R11 is 2-pyrrolidinyl, and exemplified the structurally analogous compounds of the claims, see col. 22 example 8 , col. 26, example 17. Harrison et al. taught similar compounds as Baker et al. , see '989 col. 2-4, with more explicit exemplification of the genus with variation of the heterocyclic moieties corresponding to the R11 of the instant, especially, the 1-pyrrolidinyl with variations of linking options (see RN 160376-60-3, 160376-63-6)

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art is that instead of an N-CO amide linkage (RN 160376-60-3) or NCO-CH2 linkage (RN 160386-60-6) between the piperidinyl ring and the pyrrolidinyl ring, the prior art examples have the CO-CH2 or COO-(CH2)q linkage. COCH2 linkage has been well recognized in the art as the "bioisoster" of the NCO amide linkage (see Patani p.3170, table 48).
Generically, the Harrison et al. '989 taught that the amide bond linkage and the COO(CH2)q are alternative choices for such linker (see col. 2-3, R3 is CO-Z-(CH2)q-R12) and exemplified the Z is O, q is 2 compound.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of the above references would be in possession of the attributes of the analogous compounds including the well exemplified heterocyclic moieties and generic linkers being explicitly taught by Baker and Harrison. The modification of the well exemplified compounds in the prior art with the well known conventional bioisosteric replacements prima facie obvious since bioisosteric modification has been suggested by artisan in the field to be a rational approach in drug design (see Patani et al. whole article) and such modification is often considered to be qualitative and intuitive (p.3147), thus, prima facie obvious. In the instant case, the analogous species for the described genus of Harrison have been explicitly and implicitly exemplified with representative examples of each Markush elements (see CA delineation and examples 1-90 of '898).

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paliwal et al. US 2003/0158173.

Determination of the scope and content of the prior art (MPEP §2141.01)

Paliwal '173 disclosed analogous compounds as the claims, see p.34-38.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the compounds of Paliwal '173 and the instant claims is that the substituents were on different positions of the central piperidine ring, 2,5- vs the 1,4 –of the instant.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

Position isomerism has long been recognized being a tool for obtaining more compounds for analogous use (see In re Dillon 16 USPQ2d 1897, Exparte Engelhardt 208 USPQ 343, In re Mehta 146 USPQ 284). Especially, in the instant case, the instant compounds and the prior art are for "identical" use. Position isomerism is "close" structural relationship which rendered the compounds prima facie (see In re Dillon).

6. Claims 1-18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of copending Application No. 10/321,687 in view of Patani. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reason:

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Determination of the scope and content of the prior art (MPEP §2141.01)

Paliwal '173 claimed analogous compounds as the claims, see claims 1-19, and 26-27.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the compounds of Paliwal '173 and the instant claims is that the substituents were on different positions of the central piperidine ring, 2,5- vs the 1,4 –of the instant.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

Position isomerism has long been recognized being a tool for obtaining more compounds for analogous use (see In re Dillon 16 USPQ2d 1897, Exparte Engelhardt 208 USPQ 343, In re Mehta 146 USPQ 284). Especially, in the instant case, the instant compounds and the prior art are for "identical" use. Position isomerism is "close" structural relationship which rendered the compounds prima facie (see In re Dillon).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Nov. 8, 2004

Celia Chang
Primary Examiner
Art Unit 1625